CONTROL MEASURES FOR PNEUMOCOCCAL DISEASE AND ANTIBIOTIC RESISTANCE

IN THIS CHAPTER

---

1. Opportunities for State-Level Data in Prevention and Control Work

State public health professionals may have more opportunities to effectively communicate the threat of antibiotic resistance by using local data that describe local resistance patterns, identify areas of the population in which vaccine use is below goal, and promote judicious use of antibiotics in the community. Currently, only a few states use local antimicrobial resistance surveillance data in state-based prevention and control activities. Surveillance personnel collect data using various methods and these data are then integrated into prevention campaigns. The following examples illustrate how some states have elected to use state-based surveillance of pneumococcal antimicrobial resistance data to reach their local audiences:

- Tennessee uses an active, population-based surveillance system, as part of the ABCs system, to provide data on rates of resistance in participating counties.

- The Wisconsin Antibiotic Resistance Network (WARN), supported in part by a cooperative agreement with CDC, uses enhanced, passive surveillance to collect invasive isolates that are sent to the state laboratory for susceptibility testing. Wisconsin reports 80%-90% of laboratories regularly participate in the system. Results of the susceptibility testing are routinely included in WARN newsletters and reports.
- South Carolina's Careful Antibiotic Use campaign surveys a sample of clinical laboratories and includes all pneumococcal isolates. Data are subsequently aggregated to produce county-specific resistance rates.
- North Carolina utilizes an annual survey requesting antibiogram data from all non-specialty hospitals in the state and aggregates data to provide statewide resistance rates.

Local data from these systems has been successful in raising public awareness, targeting resources and activities, developing and informing treatment guidelines, monitoring trends, and motivating behavior change by clinicians.

2. Pneumococcal Disease Vaccines

Pneumococcal Polysaccharide Vaccine (PPV)

Invasive pneumococcal disease typically affects the very young, the elderly and individuals who are immune compromised. Resistant infections are also most common in young children and the elderly. As pneumococcal infections become increasingly difficult to treat because of resistance, a high priority should be placed on preventing disease by increasing use of the 23-valent pneumococcal polysaccharide vaccine among persons at high-risk 2-64 years and individuals aged 65 and older and by the use of the 7-valent conjugate vaccine in children. (1,2,3)

A pneumococcal polysaccharide vaccine (PPV) targeting 23 of the most common serotypes of *S. pneumoniae* has been available since the early 1980s. Of 90 known capsular types of pneumococcal bacteria, the 23 types in PPV account for approximately 90% of bloodstream infections in the United States. (4) PPV has been shown to be safe and effective against invasive disease. (5,6,) The vaccine is both cost effective and protective against invasive pneumococcal infection when administered to immunocompetent persons aged greater than or equal to 2 years. Therefore, all persons who fall within appropriate high-risk categories should receive the 23-valent pneumococcal polysaccharide vaccine. (7)

The Advisory Committee on Immunization Practices (ACIP) recommends that a dose of polysaccharide vaccine should be administered to all persons aged $\geq$ 2 years at increased risk of serious pneumococcal infection because of underlying medical conditions and to all persons $\geq$ 65 years of age. (8) A single revaccination after at least 3-5 years (a minimum of 3 years if <10 years old, 5 years if 10 or more years of age) should be considered for persons aged 2-64 years who are at highest risk or likely to have rapid declines in antibody levels. This includes those with functional or anatomic asplenia, HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome or immunosuppression (e.g. organ transplants or receiving chemotherapy). Previously vaccinated persons should be vaccinated again at 65 years of age, providing at least 5 years has passed since the first dose. Pneumococcal vaccine may be administered concurrently with influenza vaccine by separate injection in the opposite arm. Children 2-4 years of age with high-risk medical conditions should receive PPV at least 2 months after receiving recommended pneumococcal

conjugate vaccine (PCV7) doses.(9) Further information on the PPV vaccine and recommended vaccination schedule for adults may be found at http://www.cdc.gov/nip/recs/adult-schedule.htm.

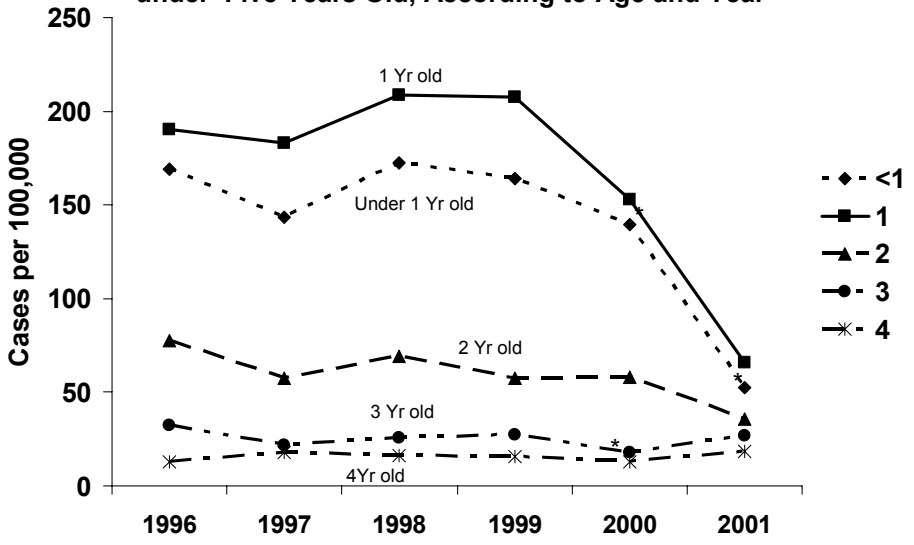
Despite its availability and payment provided under Medicare, PPV is underutilized. In 1999 only 54.1% of persons ≥65 years of age had ever been vaccinated, with particularly low coverage among African-Americans and Hispanics.(10) There also has been very low PPV coverage among persons aged 18-64 years with medical conditions placing them at high risk for serious pneumococcal infection. (11)

Pneumococcal Polysaccharide-Protein Conjugate Vaccine

The Advisory Committee on Immunization Practices (ACIP) recommends that the pneumococcal conjugate vaccine (PCV7) be provided to all children aged ≤23 months and to children aged 24-59 months who are at increased risk for pneumococcal disease (e.g., children with sickle cell disease, cochlear impants, CSF leak, human immunodeficiency virus infection, and other immunocompromising or chronic medical conditions). (12) ACIP also recommends that the vaccine be considered for all other children aged 24-59 months, with priority given to a) children aged 24-35 months, b) children who are of Alaska Native, American Indian, and African-American descent, and c) children who attend group day care centers. The conjugate vaccine has not been studied sufficiently among older children or adults to make recommendations for its use among persons aged ≥ 5 years. Persons ≥ 5 years should continue to receive 23-valent polysaccharide vaccine in accordance with previous ACIP recommendations.

PCV7 has reduced the burden of invasive disease in young children, the vaccine target audience, and may be reducing the disease rate among adults. In 2001, the rate of invasive disease among children under two years of age was 69 percent lower than in 1998 and 1999. (13) Declines in disease rates were also observed among adults (a decline of 32 percent for those 20 to 39 years old, 8 percent for those 40 to 64 years old, and 18 percent for those 65 years old or older). Data also indicate that conjugate vaccine is an effective tool for preventing infections caused by drug-resistant strains; 35 percent fewer infections due to penicillin-nonsusceptible strains occurred in 2001 than in 1999.

Figure 1: Rates of Invasive Pneumococcal Disease among Children under Five Years Old, According to Age and Year



Source: Whitney CG, et al. N Engl J Med 2003; 348:1737-46.

Data are from the Active Bacterial Core Surveillance from 1996 through 2001. The 1996 and 1997 rates do not include data from New York State.

3. Surveillance of Adverse Events Following Vaccination

Although PCV7 is highly effective, some cases following PCV7 vaccination are to be expected. Vaccine efficacy was 97% for invasive disease with pneumococcal serotypes included in the vaccine and 89% for all serotypes. For cases that do occur in vaccinated children, the Respiratory Diseases Branch (RDB) of CDC has developed a tracking system to determine the serotype of invasive pneumococcal isolates, record hosts conditions that may contribute to PCV7 failure, and to monitor for vaccine lots that may be associated with decreased protection. The tracking system is consistent with the 2000 CSTE position statement on invasive pneumococcal infections, which recommends that state health departments monitor invasive pneumococcal disease in children less than 5 years old.

The *Pneumococcal Conjugate Vaccine Failure Case Report Form* may be submitted when the following five conditions are met:

- The child is <5 years old
- The child has an invasive pneumococcal infection, defined as isolation of *S. pneumoniae* from a normally sterile site (e.g., CSF, blood, joint fluid, pericardial fluid)
- A pneumococcal isolate is available for serotyping,
- A PCV7 vaccine history is available, and
- The child has received at least one dose of PCV7

If all five conditions are met, a completed PCV7 failure case report form, lab form and isolate should be sent to the CDC Streptococcus laboratory through your state health department laboratory. The CDC disease reporting instruction sheet and case report form are available on

line at http://www.cdc.gov/nip/diseases/pneumo/PCV-survrpts/PCV7-instructions.htm. Cases of suspected PCV7 failure may also be reported to the Vaccine Adverse Events Reporting System (VAERS) at http://www.vaers.org. Reporting through VAERS is not required. However if a clinically significant adverse event occurs after vaccination with PCV7, it should be reported through VAERS. Isolates will be serotyped and results of the serotyping will be returned to the state health department and submitting physician or laboratorian.

4. Promoting Appropriate Antibiotic Use in the Community

With the emergence of antimicrobial resistance, the use of antimicrobial drugs has increased in both inpatient (14) and outpatient settings (15,16). Although the overall prescribing rate for antibiotics by office-based physicians in the United States did not change from 1980 through 1992, the prescribing rate for children rose by 48% (17), and in 1992, antimicrobial agents were prescribed second in frequency behind cardio-vascular-renal drugs in physicians' offices (18).

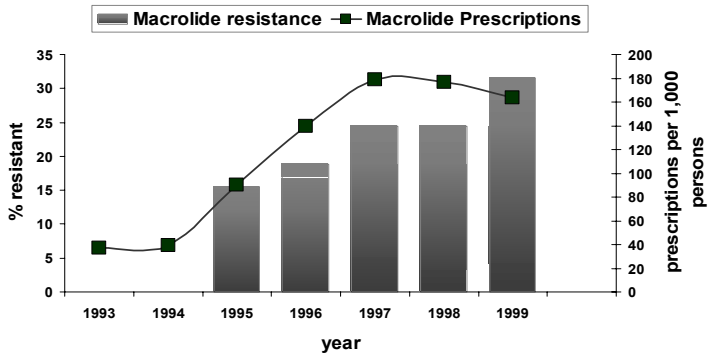
Many factors contribute to the inappropriate prescribing patterns and consumer demands of antibiotics leading to community-level resistance issues. Leading factors include:

- Prescribing antibiotics for viral infections
- Prescribing the wrong type of antibiotic
- Patient demanding antibiotics for illness
- Patients not adhering to antibiotic prescription dosing schedule or not completing a medication course

- Patients using leftover antibiotics or sharing antibiotics with family members or friends
- Pressure on health care providers to shorten visit times with patients.

Antimicrobial use, whether appropriate or inappropriate, promotes individual and community-level antimicrobial resistance. The increasing use of azithromycin, clarithromycin, and fluoroquinolones for minor illnesses or inappropriate settings warrants concern in light of the importance of these agents in the treatment of patients hospitalized with pneumonia, and the rise in macrolide- and fluoroquinolone-resistant pneumococci. (19).

Figure 2: Macroloide resistance among invasive *Streptococcus pneumoniae* isolates and macrolide use for children < 5 years of age by year



Source: Hyde T. JAMA 2001; 286;1857-62

Community-based intervention programs have played an integral role in delivering the message of the threat of antibiotic resistance to local communities. One component of CDC's broad based efforts to prevent antimicrobial resistance is a campaign to promote the appropriate use of

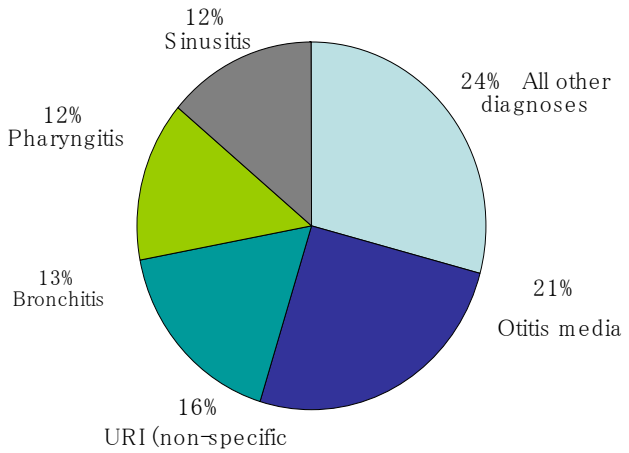
antibiotics in the community for upper respiratory infections. This campaign is comprehensive and extensive and targets both consumers and healthcare providers.

The CDC National Campaign to Promote Appropriate Antibiotic Use in the Community was launched in 1995. In 2003, this program was renamed the "Get Smart Campaign" and promoted through a national media campaign. The campaign aims to reduce the spread of antibiotic resistance by:

1. promoting adherence to appropriate prescribing guidelines among providers,
2. decreasing demand for antibiotics for viral upper respiratory infections among healthy adults and parents of young children, and
3. increasing adherence to prescribed antibiotics for upper respiratory infections.

The campaign targets the five respiratory conditions that account for a great majority of antibiotic prescriptions: otitis media, sinusitis, pharyngitis, bronchitis, and the common cold.

Figure 3: Outpatient Antimicrobial Therapy, U.S. (percentage of courses in 1992)



Source: McCaig, JAMA 1995;273:214

5. Program Activities of CDC's "Get Smart" Campaign

Educational Materials

One of the first efforts of the Get Smart Campaign was to develop and distribute clinical principles for appropriate use of antibiotics. Since antibiotic drug prescription rates are particularly high among children, pediatric guidelines were developed in collaboration with the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP). In 2001, CDC collaborated with members of AAFP, the American College of Physicians and the American College of Emergency Physicians to develop principles for appropriate antimicrobial use for adult upper respiratory tract infections.

Following the development of the pediatric and adult guidelines, CDC produced a series of health education materials for both consumers and providers to encourage appropriate antibiotic use. These materials are available at the CDC Get Smart Web site – www.cdc.gov/getsmart.

For providers:	*For the public*:
Pediatric and adult detailing sheets	Brochures
Symptomatic therapy prescription pads	Question & Answer fact sheets
Childcare excuse letter	
Wall posters	

Funding for State and Local Campaigns

In the summer of 2000, CDC distributed federal funds to eight sites for interventions to reduce inappropriate antibiotic use. In the summer of 2001, CDC was able to increase the number of funded sites to nineteen. As of 2003, twenty-seven sites received federal funding for state-based appropriate antibiotic use campaign activities. Each site develops and implements health communication and behavior change interventions to promote appropriate antibiotic use. Sites use a variety of approaches including: computer education modules, media campaigns, development of low literacy materials, provider trainings, training of volunteers as educators, building community coalitions, and education in child care settings. CDC provides support in the planning, implementation, and evaluation of these community-based interventions.

National Media Campaign

Get Smart's latest national media campaign, using the tag line, "Get Smart: Know When Antibiotics Work," was launched in Fall 2003. The target audience of the campaign is parents of young children, and healthy adults. The campaign utilizes print, television, radio and outdoor media. Educational materials and toolkits will be distributed to CDC-funded sites for use in conjunction with their local campaigns.

Medical School Curriculum

In 1999, CDC funded a contract with WESTAT (a research organization) and the University of California, San Diego for the development of a curriculum to teach medical students about the appropriate use of antibiotics in hospital and outpatient settings. This curriculum will be part of a larger curriculum for fourth-year medical students that will teach concepts from basic science in the context of clinical care.

HEDIS *Performance Measures*

One mechanism for highlighting the importance of specific medical practices, such as appropriate antibiotic use, is the public reporting of performance on selected quality of performance measures. The most widely used system of performance measures, the Health Plan Employer Data and Information Set (HEDIS), is means for raising public awareness and improving medical practice. As a measure to address inappropriate prescribing of antibiotics by clinicians, CDC and the National Committee on Quality Assurance have written two new measures, which will be a part of HEDIS in 2004. The measures will assess the appropriate

treatment of children with pharyngitis and those with upper respiratory infections. The pharyngitis measure attempts to increase the proportion of children who are tested for group A strep before receiving antibiotics for sore throat. The upper respiratory tract measure aims to decrease the proportion of children who receive an antibiotic for the common cold.

6. Developing Health Awareness Campaigns

CDC advises new programs to form a coalition as a first step in appropriate antibiotic use efforts. A coalition of diverse partners at the local level may include public health departments, health plans, professional provider organizations, school nurses, parent teacher associations, child care providers, pharmacies and pharmaceutical manufacturers. Partners bring a wealth of resources to local campaigns including knowledge of and access to target populations.

7. Additional Campaigns Targeting Antibiotic Resistance

CDC's National Center for Infectious Diseases Antimicrobial Resistance Web site can direct you to other antibiotic resistance prevention programs described below

Web site: www.cdc.gov/drugresistance.

Campaign to Prevent Antimicrobial Resistance in Healthcare Settings Launched by the Division of Healthcare Quality Promotion, the 12-Step Campaign aims to prevent antimicrobial resistance in healthcare settings. The campaign centers on four main strategies: prevent infection, diagnose and treat infection, use antimicrobials wisely, and prevent transmission.

Web site: www.cdc.gov/drugresistance/healthcare/default.htm.

Active Bacterial Core Surveillance (ABCs) At ten Emerging Infections Program (EIP) sites, ABCs tracks invasive bacterial disease caused by pathogens of public health importance. For each case of invasive pneumococcal disease in the study population, ABCs personnel complete a case report with basic demographic information and, in most cases, bacterial isolates are sent to CDC for laboratory study including testing for antimicrobial resistances.

Web site: www.cdc.gov/ncidod/osr/EIP.htm and

www.cdc.gov/ncidod/dbmd/abcs/default.htm

National Antimicrobial Resistance Monitoring System (NARMS) Because antimicrobials are given to food-producing animals, antimicrobial resistance can be transmitted to humans through the food supply. Thus, antimicrobial resistance data from people are important for public health leaders who develop regulatory policy to reduce the use of drugs in food-producing animals. The main activity of NARMS is to monitor antimicrobial resistance of human enteric bacteria. NARMS is developing a veterinary school curriculum to educate students about the use of antimicrobials in livestock and the connection to antimicrobial-resistant foodborne infections in people. Other projects include: 1) the study of dairy and swine industries to explore alternatives to antimicrobial use as growth promotants, and 2) a state-based initiative to assess antibiotic resistance trends, 3) a program to enhance collaboration between the medical, public health and veterinary communities, and 4) efforts to provide training to the veterinary community.

Web site: www.cdc.gov/narms

National Immunization Program The National Immunization Program (NIP) provides leadership for the planning, coordination, and implementation of immunization activities nationwide, and is also concerned with antibiotic resistance. Treating pneumococcal infections with penicillin and other antibiotics used to be very effective, but as bacteria have become resistant to these antibiotics, immunization against pneumococcal disease has become critical. Web site: www.cdc.goc/nip/default.htm

References

1. Sisk JE, Moskowitz AJ, Whang W, et al. Cost-effectiveness of vaccination against pneumococcal bacteremia among elderly people. JAMA 1997; 278:1333-1339.

2. Nichol KL, Baken L, Wuorenma J, Nelson A. The health and economic benefits associated with pneumococcal vaccination of elderly persons with chronic lung disease. *Arch Intern Med*. 1999; 159:2437-2442.

3. American College of Physicians Task Force on Adult Immunization. Infectious Diseases Society of America. Guide for adult immunization. Philadelphia: American College of Physicians, 1994.

4. Butler JC, Hofmann J, Cetron MS, et al. The continued emergence of drug-resistant Streptococcus pneumoniae in the United States: an update from the Centers for Disease Control and Prevention's Pneumococcal Sentinel Surveillance System. *J Infect Dis*. 1996; 174:986-993.

5. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR *Morb Mortal Wkly Rep*. 1997. 46:1-24.

6. CDC. Influenza and pneumococcal vaccination levels among persons aged $\geq$ 65 years, United States, 1999. MMWR *Morb Mortal Wkly Rep.*

7. American College of Physicians Task Force on Adult Immunization. Infectious Diseases Society of America. Guide for adult immunization. Philadelphia: American College of Physicians, 1994.

8. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR *Morb Mortal Wkly Rep*. 1997. 46:1-24.

9. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR *Morb Mortal Wkly Rep*. 1997. 46:1-24.

10. CDC. Influenza and pneumococcal vaccination levels among persons aged ≥ 65 years, United States, 1999. MMWR *Morb Mortal Wkly Rep.*

11. Singleton JA, Greby SM, Wooten KG, et al. Influenza, Pneumococcal and Tetanus Toxoid Vaccination of Adults- United States, 1993-1997. *MMWR* 2002; 49:39-62.

12. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR *Morb Mortal Wkly Rep*. 1997. 46:1-24.

13. Whitney CG, Farley MM, Hadler J, Harrison LH, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med* 2003; 348: 1737-46.

14. McCaig LF, Besser RE, Hughes JM. Trends in pediatric antimicrobial drug prescribing among office-based physicians in the United States. JAMA 2002: 287: 3096-102.

15. Bryant E, Shimizu I. Sample design, sampling variance, and estimation procedures for the National Ambulatory Medical Care Survey. Vital Health Stat 2 1988; 108:1-39.

16. McCaig LF, McLemore T. Plan and operation of the national Hospital Ambulatory Medical Care Survey. Vital Health Stat 1 1994; 34:1-78.

17. Koch H, Campbell W. The collection and processing of drug information. National Ambulatory Medical Care Survey, 1980. Vital Health Stat 2 1982; 2:1-90.

18. Physicians' desk reference. Montvale (NJ): Medical Economics Company, Inc; 1992.

19. McCaig LF, Besser RE, Hughes JM. Antimicrobial drug prescription in ambulatory care-settings, United States, 1992-2000. *Emerg Infect Dis.* 2003;8:432-437.

20. Hyde TB, Gay K, Stephens DS, Vugia DJ, Pass M, Johnson S, et al. Macrolide resistance among invasive Streptococcus pneumoniae isolates. *JAMA*. 2001;286:1857-62.

21. McCaig LF, Hughes J. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1996; 273:214-219.